Review Article

IRON DEFICIENCY ANEMIA AND ITS ORAL MANIFESTATION -A REVIEW

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Abstract: The oral cavity is the mirror of systemic health. Anemia is one such condition, which manifests itself in the oral cavity. According to the World Health Organization, the normal hemoglobin level for an adult male is around 13.8 g/dl and for an adult woman is around 12.1 g/dl. Anemia is defined as when the hemoglobin level in the blood is below the lower extreme of the normal range for the age and sex of the individual. Iron deficiency anemia is the most common nutritional deficiency disorder in children and women and is worldwide in distribution. It is characterised by fatigue, weakness, pallor, and koilonychias. Thus, oral physicians play an important role in diagnosis and thereby prevention of anemia, as oral manifestations may be the earliest feature of the condition.

Key-words: *Anemia, Iron Deficiency Anemia, Hemoglobin, Oral manifestations.*

1. Introduction

World Health Organization defines anemia, as hemoglobin level of less than 12 gm/dl in women and less than 13 gm/dl in men.[1] WHO estimates that globally 293 million young children suffer from anemia, among which approximately 50% are due to iron deficiency.[2] Anemia is defined by a decrease in the total amount of hemoglobin or the number of red blood cells. Iron Deficiency Anemia is a form of anemia due to the lack of sufficient iron to form normal red blood cells. Iron Deficiency Anemia is typically caused by inadequate intake of iron, chronic blood loss, or a combination of both.[3,4] Iron deficiency is the most common type among all other anemias and is frequently observed in infants and in adolescents who have menstruation.[5] The iron deficiency is the first cause of anemia. Pallor, fatigue and dyspnea are the most common symptoms of anemia. Anemia is classically associated with microcytosis and hypochromia in biological exams. Iron deficiency, inflammatory, etiologies, thalassemia and sideroblastic anemia are the origins of microcytic anemia.[6-10]

The non-specific systemic signs and symptoms of anemia include mucous membrane pallor, tachypnea, raised jugular venous pressure, flow murmurs, postural hypotension, tachycardia, tiredness, light headedness, breathlessness, vetigo, development/worsening of ischemic conditions.[11] Along with these systemic manifestations, anemia may also manifest certain oral manifestations, some of which are specific and some are non-specific to the condition which include mucosal pallor, angular chelitis, stomatitis, periodontal degeneration, dysphagia, depapillation of tongue etc.[12] The study of orofacial manifestations of these disorders is important because these orofacial signs and symptoms

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may be the first clinical presentation that alerts the dentist/hematologist to an underlying hematological disorder.[13]

2. Role of Iron in Hemoglobin Synthesis

2.1 Structure of Hemoglobin

Hemoglobin is a conjugated protein, consists of a protein combined with an iron containing pigment. The protein part is globin and the iron containing pigment is heme. Heme also forms a part of structure of myoglobin (myoglobin is oxygen binding pigment in muscles) and neuroglobin (oxygen binding pigment in brain). Iron is normally present in ferrous (Fe++) form. It is in unstable or loose form. In some abnormal conditions, the iron is converted into ferric (Fe+++) state, which is a stable form. Porphyrin is the pigment part of heme. It is formed by four pyrole rings (tetrapyrole) called, 1,2,3 and 4. The pyrole rings are attached to one another by methane (CH4) bridges. the iron is attached to N- of each pyrole ring and N- of globin molecule.Globin contains four polypeptide chains. among the four polypeptide chains,2 are alpha chains and 2 are beta chains.[14]

Iron Metabolism

The body absorbs 1 to 2 mg of dietary iron in a day, which is balanced through body processes (menstruation, sloughed intestinal mucosal cells, and other blood losses).[15] Dietary iron comprises heme iron (animal sources) and non-heme iron (vegetable and cereal sources). Heme iron bound to Hb and myoglobin is responsible for delivering oxygen to the tissues. Pancreatic enzymes digest heme to release it from the globin molecule in the intestinal lumen. this is followed by the absorption of heme iron into the enterocytes as metalloporphyrin takes place and it is further degraded by heme oxygenase-1 leading to the release of non-heme iron. Subsequently, iron is exported by the only iron exporter ferroportin, present on the basolateral aspect of the enterocyte.[16] On the other hand, non-heme iron is less well absorbed. It is absorbed by intestinal luminal cells through a specific transporter and released into the circulation wherein the binding of transferrin occurs. Transferrin receptors on erythroblasts accept iron-transferrin complexes, which undergo the process of endocytosis leading to the incorporation of iron into Hb.[17,18]

Etiology of Iron Deficiency Anemia

Iron metabolism is controlled by absorption rather than excretion. Iron is only lost through blood loss or loss of cells as they slough. Men and no menstruating women lose about 1 mg of iron per day. Menstruating women lose from 0.6 to 2.5% more per day. An average 60-kg woman might lose an extra 10 mg of iron per menstruation cycle, but the loss could be more than 42 mg per cycle, depending on how heavily she menstruates.[19]

A pregnancy takes about 700 mg of iron, and a whole blood donation of 500 cc contains 250 mg of iron. Iron absorption, which occurs mostly in the jejunum, is only 5–10% of dietary intake in persons in homeostasis. Iron deficiency results when iron demand by the body is not met by iron absorption from the diet. Thus, patients with Iron deficiency anemia presenting in primary care may have an inadequate dietary intake, hampered absorption, or physiologic losses in a woman of reproductive age.[20]

Signs and Symptom

Fatigueness is a common symptom of iron deficiency anemia. Fatigue occurs due to reduced oxygen to the cells or low hemoglobin. The oxygen carrying capacity is reduced ultimately. Shortness of breath, dizziness, headache, pale skin and chest pain are the other symptoms.[21] Women are more frequently affected by anemia due to blood loss during their menstrual flow.[22] Patients with Iron deficiency anemia may have characteristic systemic symptoms such as weakness, lightheadedness, shortness of breath, and palpitations.[23] In iron deficiency, blue discoloration of sclera may be noticed (It caused due to thinning and transparency

of the collagen fibres of the sclera that allows visualization of the underlying uvea). Restless leg syndrome is seen commonly in Iron deficiency anemia.[21] Iron deficiency rapidly affects the epithelial cells thereby leading to dryness and roughness of the skin, dry and damaged hair, koilonychias and alopecia. In mild-to-moderate iron deficiency loss of tongue papillae is reported. Atrophic glossitis is also noted in severe cases.[24]

Diagnosis of Iron Deficiency Anemia

The initial examination of anemia follows a simple process widely used in hematology.[25]The evaluation of the primary reason for anemia includes a complete blood count (CBC), peripheral blood smear, reticulocyte count, and serum iron indices. A CBC can be helpful in determining the mean corpuscular volume (MCV), which measures the average size of RBCs, and mean corpuscular hemoglobin concentration, which measures the concentration of hemoglobin in a given amount of packed RBCs. the common characteristics of IDA include hypochromic RBCs, microcytic, and low iron stores. Although microcytic anemia is characterized by small red blood cells and iron deficiency, up to 40% of patients with IDA have normocytic RBCs.[26,27] Other reasons of microcytic anemia include chronic inflammatory diseases, thalassaemia, lead poisoning, and sediroblastic anemia.[28] The red cell distribution width (RDW) is a measure used in combination with the MCV to differentiate between mixed causes for anemia from that of a single cause. An elevated RDW value signifies a variation in the size of the red blood cell. In addition, RDW may also be elevated at the early stages of IDA and folate with or without the deficiency of vitamin B12, both of which cause macrocytic anemia.[26,29] White blood cell (WBCs) and platelet counts help to distinguish isolated anemia from pancytopenia.[25] Patients suspected to have IDA should undergo iron studies test. The results determined from this test should be correlated with the red cell indices. The serum ferritin level is the most commonly available and useful index of iron deficiency.[30] Iron studies diagnostic for IDA consists of low hemoglobin (<13g/dL and 12g/dl in women). low transferrin saturation (<15%), a low serum ferritin (<30μg/L/l) and high total iron-binding capacity y (>13.1 μmol/l).[31,32]

However, one point to be noted is that ferritin is also an acute-phase protein and tends to be elevated in cases of infection, liver disease, inflammation, and malignancy. this can result in misleadingly elevated ferritin levels in iron-deficient patients with co-excising systemic illness. [33,31] Other markers such as C-reactive protein (CRP) may also help identify coexisting inflammation in cases of an underlying inflammation or infection.[34,35] Serum iron levels have significant diurnal variation, they tend to be low in both inflammation and IDA, and should not be used as a mode of diagnosis for iron deficiency.[30] Soluble transferrin receptor (sTfR) level is considered an additional iron index is the, which acts as a parameter for the diagnosis of IDA and as an indirect measure of erythropoiesis. It tends to be increased in patients with ID.[36]

Management of Iron Deficiency Anemi

Once IDA is confirmed, the choice between intravenous and oral forms of iron therapy should be made based on the clinical circumstances on a case basis.

Dietary Therapy

Increasing dietary iron consumption alone is insufficient to treat IDA and higher supplemental doses of iron are essential. However, increasing the iron intake and enhancing the absorption by minimizing the inhibitors and maximising the enhancers may be valuable for secondary prevention of iron deficiency.[30]

Oral Iron Therapy

The dosage of iron required to treat IDA in adults is 120 mg/day for three months; the dosage for children is 3 mg/kg per day, up to 60 mg/day.28 In a study done by Baker et al. an increase in hemoglobin of 1 g/dl after one month on treatment showed an adequate response to treatment and confirmed the diagnosis of IDA. In adults with IDA, the treatment should be continuously undergone for three subsequent months after the anemia is corrected for the replenishment of the iron stores.[37]

Parenteral Iron Therapy

Parenteral treatment may be used in patients who cannot absorb or tolerate oral iron, such as those who have undergone gastrectomy, bariatric surgery, gastrojejunostomy, or other small bowel surgeries.[38] Parenteral iron therapy can offer a number of clinical advantages, especially newer formulations with better safety profiles in addition to their ability to efficiently restore the body iron stores.[39]

Oral Manifestation of Iron Deficiency Anemia

It includes, Glossitis, glossodynia, angular cheilitis, oral candidiasis, erythematous mucositis, recurrent oral ulcers and burning mouth are the common oral complaints in iron deficiency anemia.[40] Plummer Vinson syndrome is associated with iron deficiency anemia. It is also known as Patterson–Brown–Kelly syndrome. Syndrome is characterized by iron deficiency anemia along with atrophic glossitis or angular cheilitis and dysphagia due to pharyngoesophageal ulcerations and esophageal webs. It is also associated with koilonychias or spoon shape nails.[41]

Dental Consideration

Iron deficiency anemia results in oral health problems. Oral manifestations may be the earliest feature of IDA and as a dentist we can play an important role by noticing these manifestations in patients who come for dental treatment. Following are the various oral manifestations of iron deficiency anemia:

1. Angular chelitis,
2. Atrophic glossitis or Generalised oral mucosal atrophy
3. Recurrent oral ulcer
4. Erythematous mucositis
5. Candidal infection at the corners of the mouth and on tongue.
6. Glossitis has been described as a diffuse or patchy atrophy of dorsal tongue papillae, giving a smooth, glazed appearance of the tongue. This is often accompanied by tenderness or a burning sensation. Some investigators have suggested that iron deficiency predisposes the patient to candidal infection, which results in changes seen at the corners of the mouth and on tongue. If the patient has any of these symptoms, he or she should be referred to his or her physician for a more thorough medical history, laboratory diagnosis, and treatment. Elective oral surgical or periodontal procedures should not be performed on patients with marked anemia because of the potential for increased bleeding and impaired wound healing. The patient should never be treated with iron until the cause of the microcytic hypochromic anemia is found and corrected or until a thorough search for the cause has proved unsuccessful.[42]

Conclusion

In conclusion, as the oral cavity reflects general health status of individual, oral manifestations may be the earliest feature of Iron deficiency anemia. Hence, since Oral physician may be the first person to recognize the presence of anemia, his role to diagnose any underlying condition & hence help the patient for proper referral & treatment. In women and children Iron deficiency anemia is a “silent killer” & as a dentist we should look at the clinical features & help in early diagnosis and prompt treatment by the physician.

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